REMARKS

FORMAL MATTERS:

Claims 27-57 are pending after entry of the amendments set forth herein.

Claims 48-49 were withdrawn from consideration as set out in the Office Action mailed June 16, 2006. As set out in detail below, rejoinder of these claims as amended is respectfully requested.

Claims 27-38, 44, and 46- 49 are amended, and new claims 50-57 are added. Support for these amendments is found in the claims as previously presented as well as throughout the specification. For example, see specification page 26, lines 3-6 ("Vascular anasmotosis" refers to a surgical procedure involving blood vessels); specification page 7, lines 11-15; page 25, lines 9-14; page 28, lines 5-7 (implantation of preserved vessel without a stent and discussing mesh framework); and page 7, line 16 to page 8, line 3; page 23, line 25 to page 24, line 1; page 26, lines 9-11 (composition relating to canister containing preserved vessel).

No new matter has been added.

INTERVIEW SUMMARIES

A great gratitude is owed to Examiner Isabella for his time and courtesy during the in-person interview with the inventor, Dr. James Schneider and the undersigned on October 17, 2006, as well as the subsequent telephonic interview with the undersigned on December 5, 2006.

All rejections of record were discussed, and claim amendments were discussed, including the amendments as presented here. The arguments presented previously were discussed.

The Examiner kindly agreed to again take into consideration all arguments presented, and further consider the data submitted with the 37 CFR §1.132 declaration executed by the inventor, Dr. Schneider, and filed February 1, 2005.

Again, Applicant is grateful to Examiner Isabella for his kindness to Dr. Schneider in explaining the present rejections. Applicant also thanks Examiner Isabella for his dedication to a thorough and fair examination of the present claims.

ELECTION/RESTRICTION

The Office has asserted that newly submitted claims 48 and 49 are directed to an invention that is independent or distinct from the invention originally claimed since the method of claims 48-49 do not require the specific product of claims 27-47. The Office then indicated that claims 48-49 were considered to be withdrawn as being directed to a non-elected invention. This restriction requirement is respectfully traversed.

Claim 48 as amended is directed to a method of using a preserved vessel. The preserved vessel in claim 48 includes all the limitations of the preserved vessel of claim 38. Claim 49 depends from claim 48. Accordingly, the methods of claims 48-49 are directed to use of the specific product of a previously examined claims.

Withdrawal of this restriction requirement and consideration of all pending claims on the merits in the instant application is respectfully requested.

REJECTIONS UNDER §103(A)

Pratt in view of Dardik – claims 27-34 and 38-44

Claims 27-34 and 38-44 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pratt (Publications Laryngoscope 96:1986; and 29th Ann. Meeting of Amer. Society for Head and Neck Surgery: 1987) in view of Dardik (US 3,974,526).

These rejections are respectfully traversed as applied, and as they may be applied to the presently pending claims.

The legal standard for *prima facie* obviousness is set out in MPEP § 2143:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.
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> The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

A *prima facie* case of obviousness is not established if any one of the three basic criteria is not met.

The Office Action states the following in support of the §103(a) rejection in the Office Action (text bridging pages 3-4):

> The publications to Pratt discloses the use of freeze-dried microarterial allografts that have reduced immune response when implanted. In each of the publication, Pratt suggests that [freeze] dried placental vessels should be explored as microarterial grafts. * * * It is clear from the studies of Pratt and Chow that freeze dried tissues prevent immune response.
>
> Dardik, et al teaches that placental and umbilical tissues have been used as a source for microarterial vessels for reconstructive surgery. In 1976, the current skill in the art was to chemically modify the vessels from the umbilical cord by tanning to remove surface antigens. It has been found that the tanning chemicals themselves modify the surface of the treated vessels so as to, inherently cause immune response. In light of the teachings of Dardik, et al, to use the vessels derived from placental and/or umbilical tissues as a source of microarterial allografts that can be freeze-dried to yield a reconstructive allograft that exhibits low immune response would have been obvious to one of ordinary skill in the art at the time of the invention thereof.

The Examiner clarified in the Office Action at page 5 that Dardik is cited "simply to establish that use of vessels derived from placental and umbilical tissues have been used as a source for microarterial graft." In the Office Action at pages 5-6, the Examiner explains the disclosure of Dardik relied upon for the rejections:

> Examiner's reliance on Dardik, et al is simply to establish that use of vessels derived from placental and umbilical tissues have been used as a source for microarterial graft. While Dardik et al uses chemical treatment to reduce antigenic properties of the isolated vessels, Pratt clearly established, prior to the invention herein that lyophilization of vessels reduces the vessel's immune response especially as used as an allograft. Examiner is not suggesting to substitute or use the chemical method of Dardik in combination with lyophilization for as a method for treating the vessel to reduce immunogenicity combination of the prior art as applied teach/suggest all the claim limitations.

Applicant thanks the Examiner for this clarification.

The Examiner also explained in the Office Action that he disagreed with applicant's assertion regarding that it is surprising that grafts having the recited characteristics of low antigenicity, high patency and integrity could be produced from umbilical and placental vessels (e.g., the art did not provide a reasonable expectation of success to arrive at grafts having the recited characteristics). The Office Action states at page 6:

> Applicant argued that the Office has failed to establish a prima facie case of obviousness for failure to meet at least one of the three required criteria set out above - namely, reasonable expectation of success. Examiner respectfully, disagrees with applicant's assertion. It is clear that lyophilization of vascular vessels including those derived from the placenta have achieved success in reduction of immunogenicity. Examiner contends that at the time of the invention thereof, it has been clearly demonstrated by Pratt and Chow (and others) that lyophilization is successful in reducing the immune response to treated vascular vessels, especially as used as an allograft. Moreover, Chow study indicated that lyophilized placental vessels were successful as a source for microarterial graft exhibiting reduced immunogenicity. Examiner maintains that the prior art points to a reasonable expectation of success in using lyophilized umbilical vessels as a source for microarterial graft.

Applicant respectfully submits that the statements above only speak to one of the three required characteristics recited in the claims – low antigenicity – and do not address either high patency or integrity. It is the integrity of the claimed grafts that applicant asserts to be surprising and unexpected from the disclosure of the cited art.

As discussed during the interview, and as presented in the prior arguments, the Pratt articles are concerned with non-human vessels that are derived from either rat carotid arteries or rabbit femoral and brachial arteries. After freeze-drying and rehydration, these vessels are implanted into rats and into rabbits, respectively. The grafts of Pratt were thus subjected to blood pressure that was about the same or less than the blood pressure to which the vessels used to make the grafts had been subjected naturally. The grafts were not subjected to a blood pressure significantly greater than that to which the starting vessels had been subjected. Thus Pratt did not and would not have met with this problem. This is, perhaps, why Pratt states:

> Eventually, it is anticipated that freeze-dried placental or donor vessels could be used in clinical trials ***if future preliminary laboratory studies*** in rabbits and larger animals ***are successful***.[1]

(emphasis added)

Dardik's success in use of chemically treated ("tanned") umbilical vessels as grafts does not predict success in use of freeze-dried umbilical or placental vessels as grafts. Throughout the reference, Dardik points out that the chemical treatment results in "hardening" of the vessel. Indeed, the terms "hardening agent" and "tanning agent" are used interchangeably. See, e.g., Dardik at col. 4, lines 7-8 and lines 38-42. Dardik's process thus imparts a change in the structure of the vessel. Because the claimed grafts are not subjected to chemical treatment, whatever effect on graft integrity that may be provided by Dardik's chemical treatment process is not present.

Thus, although Dardik does indeed note use of umbilical cord vessels, the process to which the vessels are subjected is very different and yields a very different product. As kindly clarified by the Examiner, Dardik only provides evidence that umbilical cord vessels have been used as a source for grafts, and provides nothing with respect to the integrity of grafts that can be produced by freeze-drying such vessels.

With respect to the §1.132 declaration, the Examiner states in the Office Action at page 7 that no evidence was presented that freeze drying placental vessels differs from freeze drying umbilical vessels. The present claims are amended to encompass both placental and umbilical vessels, rendering this issue moot.

Applicant previously argued – and still maintains – that it is surprising that freeze-dried vessels prepared as set out in the present claims have a structure that allows them to withstand at least twice or more the blood pressure than that to which the fresh tissue is subjected in nature, and thus renders them suitable for use in an adult human.[2] This feature of the claims – namely *graft integrity* when implanted

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[1] Pratt et al. 29th Ann. Meeting of Amer. Society for Head and Neck Surgery: 1987, page 11.

[2] Applicants note that while the structure of the preserved vessels is described and claimed in terms of characteristics of the preserved vessel when in use as a graft (i.e., when implanted in an adult human) it should be understood that this is not

as vascular graft in an adult human without a stent or supporting mesh framework – is not obvious from the cited art.

The Examiner pointed out both in the Office Action (page 7) and during the interview that the claims are devoid of language and limitations, and further asserted that Chow appears to indicate that the graft would have sufficient integrity and immunological properties after grafting. The Office Action states at page 8:

> Applicant's assertion that the studies above demonstrate thatumbilical cord and placental vessels can be preserved by freeze-drying according to the invention and maintain sufficient integrity to be useful as grafts in a human adult has been noted, however the statement and corresponding arguments are not commensurate with the scope of the claims.

As discussed during the interview, the claims are now amended to indicate that the characteristics of the graft – low antigenicity, high patency, and integrity – are present when implanted as a vascular graft in an adult human. This necessarily requires that the graft be adapted to exhibit the recited characteristics under conditions of adult blood pressure. Applicant respectfully submits that the scope of the amended claims is commensurate with the arguments previously presented.

As set out in the Preliminary Amendment filed February 1, 2005, prior to the work that led to the claimed invention, many uncertainties existed as to whether freeze-dried human umbilical cord or human placental vessels would maintain integrity when subjected to blood pressure of a human adult.

Human placental and umbilical cord vessels are extremely delicate. As Dr. Schneider states in his §1.132 declaration, one could not predict whether removal of umbilical cord or placental vessels followed by freeze-drying would so badly damage the vessels to render them useless. The freeze-drying process could very well have destroyed the integrity of the vessels. (Schneider Declaration, paragraph 6).

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intended to limit the scope of the claims to use of the claimed compositions as grafts in an adult humans. Rather, this claim language is intended as a way to describe the characteristics of the claimed composition.

In addition, and as discussed at length during the interview and here, vessels of umbilical cord and placenta are subjected only to human *fetal* blood pressure which is much lower than human adult blood pressure. As detailed in the §1.132 declaration, fetal blood pressure is usually in the range of about 60/25 mmHg, while healthy adult blood pressure is about 140/80 mmHg. Blood pressure associated with human adult hypertension is even greater (160/120 mmHg). Accordingly, it was surprising that grafts produced by freeze-drying umbilical cord or placental vessels would withstand *at least twice or more the blood pressure* than that to which the fresh tissue is subjected in nature. (Schneider Declaration, paragraphs 7 and 12-18)

New claims 50-57 include all limitations of the independent claims discussed above, and thus should be found patentable for at least the same reasons.

Pratt and Dardik in view of Lau and Chin - Claims 35-37 and 45-47

Dependent claims 35-37 and 45-47 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pratt in view of as applied to claims 27 and 38, respectively, and further in view of Lau (US 5,876,432) and Chin (US 5,800,540). This rejection is respectfully traversed.

The failure of the combined disclosures of Pratt and Dardik to render the claimed invention obvious is discussed above, and applies to claims 33-37 and 45-47 with equal force.

Combining Lau and/or Chin with Pratt and Dardik does not cure the deficiencies of the rejection. Lau and Chin at best only disclose particular types of stents.

Withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number SNDR-001CIP(SP).

Respectfully submitted,
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Date: Dec 13, 2006

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